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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BERCH, MARK L	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 10/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/070,791	HERDEWIJN ET AL.	
	Examiner	Art Unit	
	Mark L. Berch	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-39,41 and 43-45* is/are pending in the application.

4a) Of the above claim(s) *8,9,11,13 and 24-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,10,12,15-23,35-39,41 and 43-45* is/are rejected.

7)☒ Claim(s) *14* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *3/8/2002* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/3/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I in the reply filed on 8/20/2004 is acknowledged. The traversal is on the ground(s) that the "general inventive concept" is the cyclohexenyl moiety. This is not found persuasive because in fact, a cyclohexenyl ring is not required to be present. The ring can in fact be e.g. a benzene ring. The only fixed structural feature required to be present is the oxygen atom and the adjacent methylene carbon. However, this -O-CH_2- fragment is too small to be considered a core and is not itself responsible for the actual activity. The nucleobase is essential for antiviral activity and hence restriction is proper on the basis of its nature. This is especially true since in the area of antivirals, these are generally not interchangeable. For example, if the anti-HIV agents AZT and d4T and FLT have their nucleobase thymidine replaced with e.g. adenine, the resulting compounds are not effective against AIDS. Each of these has a different sugar-type moiety.

Applicants state: "... an Examiner is not allowed to raise a non-unity objection after the application has entered the national phase and where in the international phase no such objection has been raised." There is no such bar. Applicants go on to quote the PCT Applications Guide, paragraph 138, which states "an international application which complies with the unity of invention requirements laid down in Rule 13, must be accepted by all the designated and elected offices since Article 27.1 does not allow any national law to require compliance with requirements relating to the contents of the international application different from or additional to those provided in the PCT." The examiner has not acted in violation of such paragraph. The examiner has

determined that the application does not comply with Rule 13 for reasons previously stated. The examiner has not set forth any additional or different requirements, just Rule 13. Applicants appear to be reading this paragraph as saying that the USPTO must accept an external determination of whether Rule 13 has been complied with. That is not what the quoted language states. The PTO makes its own determination as to whether Rule 13 was complied with.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-7, 10, 12, 14-23, 35-39, 41 and 43-45 are objected to as having non-elected subject matter present. This material must be removed. Limitation to the adenines will resolve the matter.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 10, 12, are rejected under 35 U.S.C. 102(b) as being anticipated by Maurinsh, et al.

See page 2863, compound 6, corresponding to B = adenine N-protected with methoxytrityl, and R1 = trityl, X = H, Z forms cyclohexene of Formula III. Compound 5 is similar, with R1 as H.

Claim 1, 10, 12, are rejected under 35 U.S.C. 102(b) as being anticipated by Gannett et al, Hiramoto.

In Gannett, see page 299, compound 2b, corresponding to Z making this a phenyl ring. In Hiramoto, see second compound in chart 2.

Claims 1-5, 10, 12, are rejected under 35 U.S.C. 102(b) as being anticipated by Konkel, et al.

See 14 for the cis compound with R1= H, X = H, corresponding to formula II, IV, VIII, X and X'. Compound 19 on page 802 is a protected version (the carbamate). These are presumed to be a mixture of both cis isomers.

Claims 1-7, 10, 12, 14-23, 35-39, 41, 43-45 are rejected under 35 U.S.C. 102(a) as being anticipated by Wang (2000) or Wang (1999).

The references were published before the filing of the PCT application, and inventorship is different from authorship, but the same subject matter is disclosed. The rejected claims are not entitled to benefit of any of the US provisional applications. None of these applications have the scope of genus as seen in the rejected claims. For example, X = H is not seen. A great deal of material was added to the PCT application which was not in any given US provisional application.

Specification

The abstract is objected to as too vague. The Formula I structure needs to be provided. The definitions could be shortened a little for reasons of space.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any

> person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7, 10, 12, 15-23, 35-39, 41, 43-45 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. "General" is indefinite. A formula cannot be both general and specific. Deletion is suggested.
2. The scope of "purine bases" is unclear. Judging from the species present in the specification, and the wording of claim 10, applicants actually intend that the purine be substituted. Is substitution mandatory or optional, and what substituents are permitted and what substituents are not?
3. "For example" is improper alternative language (In re Kingston, 65 USPQ 371). This material is not needed for the claim.
4. The "substitute" in claim 4 should presumably be "substituted".
5. The last claim 12 choice is clearly in error. The protecting group has to be monovalent as it is attached to an oxygen; this group is divalent. Was benzyl intended? Benzhydryl? Alpha-phenethyl? For whichever choice is made, applicants must show that one of ordinary skill in the art would have known that this choice, and not another, was intended.

6. The "providing" in claim 15 is unclear. Would this cover buying it in a store? Taking it off a shelf? If a synthesis step is intended, not has been recited. The nature of the starting material and the nature of the actual step is not given.
7. In claim 16, "...type" is unclear. The addition of the word "type" to an otherwise definite expression renders it indefinite. See *Ex parte Kristensen*, 10 USPOQ2d 1701; *Ex parte Copenhaver*, 109 USPQ 118; *Ex parte Remark* 15 USPQ 2d 1498, 1500; *Ex parte Pappas*, 23 USPQ2d 1636; *Ex parte Attig*, 7 USPQ2d 1092, and MPEP 2173.05(b).
8. Claim 18 is improperly dependent on claim 15. Claim 15 makes no provision for R1 and R2 to be combined into a single substituent. The dependency of claim 18 on claim 15 makes it unclear what claim 15 really intends.
9. What would an "analogue" cover in claim 15? What would it not cover? Where is the line between an analogue of XIII and one which is not? Likewise in claim 19.
10. The dependency of claim 19 on 15 is in error, because the XIV to which it refers is in claim 19, not claim 15.
11. Does Me in claim 20 stand for metal or methyl? Either is conventional. For whichever choice is made, applicants must show that one of ordinary skill in the art would have known that this choice, and not another, was intended. Likewise claim 23.
12. A complete and proper composition claim must recite a carrier, otherwise it is just a compound claim. Hence, claim 36 is improper.

Claim 20 is rejected under 35 U.S.C. 112, paragraphs 1 and 2, as the claimed invention is not described, or is not described in such full, clear, and exact terms as to

enable any person skilled in the art to make and use the same, and/or failing to particularly point out and distinctly claim the subject matter which applicant regards as his invention. Specifically:

This reaction is impossible. Thus, it is either written wrongly (paragraph 2) or if written correctly, is not enabled (paragraph 1). Assuming that the Me is methyl, a reductive process will not remove a methyl from the methoxy of XVA, or remove the alkyl or alkenyl from the alkoxy or alkenyloxy of XVB. In fact, cleavage of such a group requires a reagent such as concentrated HBr, which will add to the ring double bond and hence would be unsuitable.

Second, the examiner cannot locate this reaction in the specification, and hence is lacks description in the specification ((paragraph 1)).

Claims 41 and 43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The way these claims are written, it constitutes a claim for the effecting of any pharmaceutical use whatsoever, without limitation. Such a scope cannot possibly be deemed enabled.

Claim 45 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for herpes viruses, does not reasonably provide enablement for viruses generally. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claim is drawn to the treatment of viruses generally. No such feat has ever been accomplished. Most antivirals are effective against only one or two viruses. Although several drugs have been developed which are effective against a handful of viruses, no one has been able to get any of these antiviral drugs to work generally. There are over 400 pathogenic viruses in humans alone, with hundreds more in animals.

Thus, it now includes rotoviruses, especially the Group A type, which commonly lead to osmotic diarrhea in children. It includes calciviruses (e.g. Norwalk, Kawaii, Snow Mountain, etc) which cause gastroenteritis and are so poorly understood that even classification of these is considered poor. It covers measles, which can lead to croup, conjunctivitis and bacterial pneumonia. It covers astroviruses and coronaviruses, including toroviruses, which commonly cause diarrhea, certain forms of the common cold, and SARS. It covers the very dangerous category of enteroviruses, which embrace the three polio viruses, around 30 Coxsackie viruses, a like number of echoviruses as well as other enteroviruses. These cause all manner of paralytic disorders, aseptic meningitis, pericarditis, etc, often with permanent damage or death, and are widespread. Rubella has serious implication for pregnant women. It also embraces reoviruses, which have been associated with encephalitis and pneumonia. It further embraces paramyxoviruses, especially mumps, which can cause edema, orchitis, pancreatitis, meningitis and testicular damage. It covers Parvoviruses, including B19, which can cause fifth disease and arthritis, and can exacerbate a whole range of blood disorders. It covers the Marburg virus, which can produce lesions practically anywhere in the body and Ebola, which is often deadly. It covers herpes viruses such as EBV, HHV-5, HHV-6 , HHV-7, HHV-8, HVS and Simian B virus, which , is capable of

infecting simian handlers, causing among other things meningoencephalitis. It covers Parainfluenza, RSV, rabies, New Castle disease, Hepatitis E, hantoviruses, and various vesiculoviruses, which can cause vesicular stomatitis. It covers alpha viruses, such as Venezuelan encephalitis or the Semliki Forest virus. It covers retroviruses such as HTLV-I, HTLV-II and FeLV. There are also dozens of phleboviruses causing a wide assortment of fevers (e.g. sandfly fever) widespread in southern Europe, middle east and Asia. Other arboviruses of some importance include various tick fevers, and Rift Valley fever. There are all manner of arboviruses which attack the CNS, including, just in the United States, SEF, EEE, WEE, and SE and numerous others elsewhere. It covers the rhinoviruses, the most common cause of the "common cold". It covers all manner of poxviruses and much, much more.

Under such circumstances, it is proper for the PTO to require evidence that such an unprecedented feat has actually been accomplished, *In re Ferens*, 163 USPQ 609. No such evidence has been presented in this case. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art, *Genentech vs Novo Nordisk*, 42 USPQ2nd 1001, 1006. When operativeness has been properly challenged, it is incumbent on applicant to limit the claims accordingly, cf. *In re Harwood*, 156 USPQ 673, *In re Cook*, 169 USPQ 298, I*n re Langer*, 183 USPQ 288, *In re Corkill*, 226 USPQ 1005, 1009, and *In re Rainier*, 153 USPQ 802.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Berch whose telephone number is 571-272-0663. The examiner can normally be reached on M-F 7:15 - 3:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on (571)272-0674. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mark L. Berch
Primary Examiner
Art Unit 1624

10/5/04